A comparison of computational models with and without genotyping for prediction of response to second-line HIV therapy

AD Revell,1 MA Boyd,2 D Wang,1 S Emery,2 B Gazzard,3 P Reiss,4,5 Al van Sighem,5 JS Montaner,6 HC Lane7 and BA Larder1

1The HIV Resistance Response Database Initiative (RDI), London, UK, 2The Kirby Institute for infection and immunity in society, University of New South Wales, Sydney, NSW, Australia, 3Chelsea and Westminster Hospital, London, UK, 4Department of Global Health, Academic Medical Centre of the University of Amsterdam, Amsterdam Institute for Global Health and Development, Amsterdam, The Netherlands, 5Stichting HIV Monitoring, Amsterdam, The Netherlands, 6BC Centre for Excellence in HIV and AIDS, Vancouver, BC, Canada and 7National Institutes of Allergy and Infectious Diseases, Bethesda, MD, USA

Objectives
We compared the use of computational models developed with and without HIV genotype vs. genotyping itself to predict effective regimens for patients experiencing first-line virological failure.

Methods
Two sets of models predicted virological response for 99 three-drug regimens for patients on a failing regimen of two nucleoside/nucleotide reverse transcriptase inhibitors and one nonnucleoside reverse transcriptase inhibitor in the Second-Line study. One set used viral load, CD4 count, genotype, plus treatment history and time to follow-up to make its predictions; the second set did not include genotype. Genotypic sensitivity scores were derived and the ranking of the alternative regimens compared with those of the models. The accuracy of the models and that of genotyping as predictors of the virological responses to second-line regimens were compared.

Results
The rankings of alternative regimens by the two sets of models were significantly correlated in 60–69% of cases, and the rankings by the models that use a genotype and genotyping itself were significantly correlated in 60% of cases. The two sets of models identified alternative regimens that were predicted to be effective in 97% and 100% of cases, respectively. The area under the receiver-operating curve was 0.72 and 0.74 for the two sets of models, respectively, and significantly lower at 0.55 for genotyping.

Conclusions
The two sets of models performed comparably well and significantly outperformed genotyping as predictors of response. The models identified alternative regimens predicted to be effective in almost all cases. It is encouraging that models that do not require a genotype were able to predict responses to common second-line therapies in settings where genotyping is unavailable.

Keywords: antiretroviral, computational model, genotype, HIV, response prediction.

Accepted 24 February 2014